Amendments to the Drawings:

The attached drawing sheet includes changes to Figure 2. This sheet, which includes Figure 2, replaces the original sheet including Figure 2. Figure 2 has been amended to provide clear, electronically reproducible text.

REMARKS

Upon entry of this amendment, claims 1 and 3-41 are pending in the instant application. Claim 3 has been cancelled herein, without prejudice or disclaimer. Claims 1, 11-17, 19-22, 25-29, and 33 have been amended. New claims 34-41 have been added. Applicants reserve the right to prosecute the cancelled subject matter, as well as the originally presented claims, in continuing applications. Support for new claims 34-41 is found at least in originally filed claims 19, 20, 21, 25, 26, and 28. Accordingly, no new matter is added.

I. Drawings

The Examiner objected to the drawings because the text in Figure 2 is difficult to read. Applicants submit a Substitute Sheet for Figure 2, to provide an electronically reproducible Drawing sheet in accordance with 37 C.F.R. 1.84(e). No new matter has been added by the amendments presented herein.

Applicants have not provided an annotated sheet showing all changes to Figure 2, as the amendments presented herein have been made solely for the purpose of clarifying the text presented therein. If the Examiner would like annotated copies of the amended drawing sheet, he is urged to contact the undersigned at the telephone number provided below.

II. Incorporation by Reference

The Examiner objected to the specification for incorporating two U.S. patents which themselves incorporate essential material by reference. The specification has been amended at page 14, lines 14-21 to include the polymeric terms present in U.S. Pat. Nos. 5,455,044 and 5,576,018. These references had been expressly incorporated by reference in the instant application, yet they, themselves incorporate material by reference. The amendatory material presented in this Amendment consists of the material present in U.S. Pat. Nos. 5,455,044 and 5,576,018, not in the material incorporated by reference by these patents. In accordance with the provisions of MPEP §608.01(p)(2), Applicants submit herewith a Declaration by the undersigned, acting as a practitioner representing Applicants in this application, to establish that no new matter

has been added by the amendments presented herein. Accordingly, Applicants request that this objection be withdrawn.

III. Specification

The Examiner objected to the disclosure based on informalities relating to capitalization of chemical terms at page 32, line 29; page 39, line 21; and a missing space at page 39, line 27. Applicants have amended the specification herein to remove the capitalization of these terms, and to insert a space between the "2.0" and the mm at page 39, line 27.

The Examiner also objected to the disclosure at page 15, line 29; page 30, line 11; page 32, line 2; page 33, line 30; and page 35, line 30 for the use of uncapitalized trademarks. These terms have been amended to the capitalized form and the generic terminology for each term has been added.

Accordingly, Applicants request that these objections be withdrawn.

IV. Claims

The Examiner objected to claims 19 and 25 because a comma was missing between the words "medications" and "enzymes". This comma has been inserted and the duplicate term "enzymes" has been deleted.

The Examiner also objected to claims 21 and 28 because the term "antibiotic delivery" was included in a list of central nervous system disorders. This term has been removed from claims 21 and 28, and new, dependent claims 34 and 35 have been added. Support for these claims can be found, at least, in claims 21 and 28 as filed.

Accordingly, Applicants request that these objections be withdrawn.

V. § 112, Second Paragraph Rejections

The Examiner has rejected claims 13-16, 19-21, 25, 26, 28, and 29 under 35 U.S.C. § 112 second paragraph as being indefinite.

Claims 13-15 were rejected for reciting the term "said ratio". This term has been amended to read "the ratio".

Claims 16 and 29 were rejected for reciting the term "cellulose derivatives". This term has been amended to read "cellulose".

Claims 21 and 28 were rejected for reciting the phrase "other types of neurological and psychiatric illnesses". This phrase has been deleted.

Claims 20 and 26 were rejected for reciting the term "non-steroidal products". This phrase has been deleted.

Claims 19 and 25 and claims 20 and 26 were rejected for including a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation. The claims were also rejected for including the phrase "such as". The sub-ranges have been removed from claims 19, 25, 20, and 26 and added in new, dependent claims 36-41.

Claim 22 was rejected as being incomplete for omitting an essential step. Claim 22 has been amended to specify that the contacting a central nervous system tissue occurs upon intrathecal administration of the composition. Support for this amendment can be found at least at page 2, lines 27-30; and page 3, lines 4-6.

As such, Applicants respectfully request that the Examiner withdraw these rejections.

VI. § 102 Rejections

Patton

Claims 1-3, 5 and 9 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,814,607 ("Patton"). Claim 3 has been canceled. Therefore, this rejection is moot as it pertains to this claim. Claim 1 has been amended herein. Claims 2, 5, and 9 properly depend from claim 1.

The Examiner states that Patton discloses compositions comprising a parathyroid hormone (PTH) fragment (a polymer) suspended in an aerosol propellant (a buoyancy agent). The PTH fragment can be co-administered with vitamin D calcitonin and/or dietary calcium supplements (therapeutic agents). See Office Action dated November 7, 2005 ("Office Action") at page 7. Thus, the Examiner states that Patton discloses all of the limitations of claims 1-3, 5, and 9. Office Action at page 8.

Applicants traverse this rejection, as the cited reference does not disclose every element of the controllably buoyant composition as now claimed. As amended, claim 1 recites a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the composition is controllably buoyant within the cerebrospinal fluid (CSF).

In contrast, the polymer disclosed in Patton is dissolved or suspended in an aerosol propellant (e.g., a hydrofluorocarbon, HFC) so that the polymer is formulated for pulmonary or respiratory administration. Patton makes no mention of a polymer particle that contains the buoyancy agent, for example an HFC. It is the inclusion of the buoyancy agent within the polymer particle that renders it controllably buoyant in the CSF. Further, while Patton discloses co-administration of a PTH protein fragment and vitamin D calcitonin and/or dietary calcium supplements, there is no mention of including such a compound within a polymeric particle.

As such, withdrawal of this rejection is requested.

Pitt

Claims 1-3, 5, 9, 16, and 20 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,354,934 ("Pitt"). Claim 3 has been canceled. Therefore, this rejection is moot as it pertains to this claim. Claim 1 has been amended herein. Claims 2, 5, 9, 16 and 20 properly depend from claim 1.

The Examiner states that Pitt discloses compositions comprising a erythropoietin (EPO) (a polymer) respirable suspension formulations comprising EPO, human serum albumin, lactose and a HFC. Thus, the Examiner states that Pitt discloses all of the limitations of claims 1-3, 5, 9, 16, and 20. Office Action at page 9.

Applicants traverse this rejection, as the cited reference does not disclose every element of the controllably buoyant composition as now claimed. As amended, claim 1 recites a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the composition is controllably buoyant within the cerebrospinal fluid (CSF).

In contrast, Pitt discloses direct administration of EPO to the lungs of a patient. The Pitt composition contains a polymer (EPO, and lactose and/or albumin) suspended in an aerosol

propellant (e.g., tetrafluoroethane) so that the polymer is formulated for pulmonary or respiratory administration. See Pitt, column 9, lines 9-10. Pitt makes no mention of a polymer particle that contains the buoyancy agent. It is the inclusion of the buoyancy agent within the polymer particle that renders it controllably buoyant in the CSF. Further, while Pitt discloses co-administration of EPO protein and albumin and/or albumin, there is no mention of including such a compound within a polymeric particle.

As such, withdrawal of this rejection is requested.

Green

Claims 1, 2, 10, 12, and 17 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,814,666 ("Green"). Claims 1 and 12 have been amended herein. Claims 2, 10 and 17 properly depend from claim 1.

The Examiner states that Green discloses compositions, useful for antiparasitic, antifungal, and antibacterial treatments, comprising a pharmaceutically acceptable carrier, including a polymer, and a therapeutically effective amount of a compound capable of releasing nitric oxide. See Office Action at pages 9 and 10. The Examiner further states that Green discloses that the nitric oxide releasing compounds, alone or in combination with other components, can be made into aerosol formulations to be administered via inhalation., which can be placed into pressurized propellants, such as nitrogen. Office Action at page 10. Thus, the Examiner states that Green discloses all of the limitations of claims 1-3, 5, and 9. Office Action at page 8.

Applicants traverse this rejection, as the cited reference does not disclose every element of the controllably buoyant composition as now claimed.

As amended, claim 1 recites a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the composition is controllably buoyant within the cerebrospinal fluid (CSF).

As amended, claim 12 recites a composition comprising a first polymeric particle having a first therapeutic agent and a buoyancy agent contained therein, and a second polymeric particle comprising a second therapeutic agent and a buoyancy agent contained therein, wherein the composition is controllably buoyant within the cerebrospinal fluid.

In contrast, Green discloses a composition comprising a carrier (e.g., a polymer) and a nitric oxide generating compound (e.g., a therapeutic agent) alone or in combination with other agents, that may be aerosolized with a propellant (e.g., nitrogen), so that the polymer is formulated for respiratory administration. See, Green, col. 5, lines 3-5; col. 12, lines 32-37. Green does not describe a polymer particle that contains the buoyancy agent, for example nitrogen, inside the particle. It is the inclusion of the buoyancy agent within the polymer particle that renders it controllably buoyant in the CSF. Further, Green does not disclose compositions comprising a first and second polymeric particle, each of which contains a therapeutic agent and a buoyancy agent.

As such, withdrawal of this rejection is requested.

Nissen

Claims 1-3, 5, 9, 16, and 20 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Publication US2002/0142964 A1 ("Nissen"). Claim 3 has been canceled. Therefore, this rejection is moot as it pertains to this claim. Claim 1 has been amended herein. Claims 2, 5, 9, 16, and 20 properly depend from claim 1.

The Examiner states that Nissen discloses compositions comprising a polypeptide or a polypeptide conjugate (biologically active polymers), optionally containing human serum albumin (a hematological agent), one or more sugar alcohols, an HFC and a surfactant. Office Action at page 11. Thus, the Examiner states that Nissen discloses all of the limitations of claims 1-3, 5, 9, 16, and 20. Office Action at page 11.

As discussed above, claim 1 recites a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the composition is controllably buoyant within the cerebrospinal fluid (CSF).

In contrast, the polymer disclosed in Nissen is suspended in a propellant with the aid of a surfactant, so that the polymer is formulated for use with a metered dose inhaler. See Nissen, paragraph 0284-0285. Nissen fails to describe a polymer particle that contains the buoyancy agent, for example an HFC. It is the inclusion of the buoyancy agent within the polymer particle that renders it controllably buoyant in the CSF.

As such, withdrawal of this rejection is requested.

Ouadji

Claims 1-2, 6, 16, 17, 19, 20, and 33 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Publication US2003/0138486 A1 ("Ouadji"). Claim 1 has been amended herein. Claims 2, 6, 16, 17, 20, and 33 properly depend from claim 1.

The Examiner states that Ouadji discloses dosage forms for improving the bioavailability of therapeutic agents that are metabolized in the upper gastrointestinal (GI) tract by formulating them in a controlled-release matrix. Office Action at page 11. These Ouadji compositions are "floating dosage forms" as they are buoyant in gastric fluid. Ouadji at paragraph 0012. The Examiner further states that Ouadji discloses various optional buoyancy agents, including celluloses, gums, polysaccharides, starch, starch derivatives, and gelatin. Office Action at page 12. Further, the buoyancy agent can be any agent that produces carbon dioxide gas when contacted with gastric acidity. Id.

Applicants traverse this rejection.

As amended, claim 1 recites a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil, and the composition is controllably buoyant within the cerebrospinal fluid (CSF).

Ouadji fails to describe a gas or oil buoyancy composition. The composition disclosed in Ouadji optionally contains a solid-form buoyancy agent (e.g., celluloses, gums, polysaccharides, starch, starch derivatives, and gelatin), preferably the buoyancy agent is a hydrocolloid (a substance that forma a gel with water, e.g., Jell-O), most preferably, the buoyancy agent is a hydroxypropylmethylcellulose. Ouadji, paragraph 0024. Ouadji further states that any agent that produces carbon dioxide gas when contacted with gastric acidity can be used to increase buoyancy. Id. Thus, a solid buoyancy agent may, upon degradation of the controlled release matrix, release a gas. However, Ouadji makes no mention of a polymer particle that contains a gas or oil buoyancy agent. A composition that is buoyant because it stably includes a gas is different than one that derives its buoyancy from releasing a gas.

As such, withdrawal of this rejection is requested.

VII. § 103 Rejections

Kim and Ouadji

Claims 1-10 and 12-31 were rejected under 35 U.S.C. 103 as being unpatentable over U.S. Patent 5,455,044 ("Kim") in view of U.S. Patent Publication US2003/0138486 A1 ("Ouadji"). Applicants note that claim 3 has been canceled herein. Therefore, this rejection is moot as it pertains to this claim. Independent claims 1, 12 and 22 have been amended herein. Claims 2, 4-10 and 16-21 properly depend from claim 1. Claims 13-15 depend from claim 12. Claims 24-30 depend from claim 22.

According to the Examiner, Kim discloses a method for treating a neurological disorder using a slow-release vehicle for delivery of a therapeutic agent to the cerebrospinal fluid (CSF) of a human, and that the surprising ability to ameliorate a neurological disorder using the Kim methods is because the agent is allowed to persist in the cerebro-ventricular space. Office Action at page 14. The Examiner further states that Kim lacks the explicit teaching of compositions comprising a buoyancy agent and specific gravity values. Office Action at page 16.

The Examiner has stated that "it would have been obvious to one of ordinary skill at the time of the instant invention to combine the teachings of Kim and Ouadji, because both inventors describe dispersible pharmaceutical compositions comprising therapeutic agents and polymers, which have controlled-release or sustained-release properties. A skilled artisan would have been motivated to combine the teachings of Ouadji and Kim, to affect the density of Kim's formulations through the use of buoyancy agents, including formulations that would generate CO_2 gas in situ upon degradation of the polymer matrix." Office Action at page 16 .

Applicants traverse this rejection, as the cited combination of references does not disclose or suggest every element of the claimed compositions.

Claim 1

As amended, claim 1 recites a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and the composition is controllably buoyant within the cerebrospinal fluid (CSF). Claims 2, 4-10 and 16-21 properly depend from claim 1, and necessarily contain all of the limitations set forth in this independent claim.

The Kim reference does not disclose or suggest a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and the composition is controllably buoyant within the cerebrospinal fluid. The Ouadji reference fails to remedy the deficiencies in the teachings of Kim, because it also does not describe the buoyancy agents recited in the amended claims.

Kim does not describe the use of a gaseous buoyancy agent contained within a polymeric, particle, and moreover, controllable buoyancy is not suggested by Kim or the cited combination of references. Kim simply discloses a polymeric dispersion system for use in the CNS. There is no disclosure to point one skilled in the art to the desirability of controlling the buoyancy of the dispersion system. Indeed, the only mention of density refers to the density of the materials used in the process for production of the dispersion system:

> Polymeric dispersion systems can be prepared by a process similar to the coacervation of microencapsulation. If desired, the density of the dispersion system can be modified by altering the specific gravity to make the dispersion hyperbaric or hypobaric. For example, the dispersion material can be made more hyperbaric by the addition of iohexol, iodixanol, metrizamide, sucrose, trehalose, glucose, or other biocompatible molecules with high specific gravity.

Kim at column 3, lines 41-49 (emphasis added).

The IUPAC Compendium of Chemical Terminology 2nd Edition (1997) defines coacervation as the "separation into two liquid phases in colloidal systems. The phase more concentrated in colloid component is the coacervate, and the other phase is the equilibrium solution." 1972, 31, 611.

Thus, Kim is concerned with the density of the particle population during the process of producing the microspheres themselves. There is no teaching or suggestion of the desirability of modulating, or even considering, the density of the formed particles relative to the CSF. There is no reason for one to look to the art of improving the bioavailability of agents in the GI tract to modify the density of agents administered to the CNS. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. *Alza Corp. v. Mylan Laboratories Inc.*,

391 F.3d 1365, 1372-1373 (Fed. Cir. 2004). Here, neither reference provides the requisite motivation.

Moreover, even if the combination were proper, Ouadji does nothing to cure the deficiencies of Kim. As described above, Ouadji states that any agent that produces carbon dioxide gas when contacted with gastric acidity can be used to increase buoyancy. Ouadji, paragraph 0024. Thus, a solid buoyancy agent may, upon degradation of the controlled release matrix, release a gas. However, Ouadji makes no mention of a polymer particle that contains a buoyancy agent that is a gas or an oil, and there is no indication that his compositions would be controllably buoyant in the CNS, a composition that is markedly different from stomach fluids.

Accordingly, Applicants submit that a *prima facie* case of obviousness has not been established. As such, withdrawal of this rejection is requested.

Claim 12

As amended, claim 12 recites a composition comprising a first polymeric particle having a first therapeutic agent and a buoyancy agent contained therein, and a second polymeric particle comprising a second therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agents are each a gas or an oil, and the composition is controllably buoyant within the cerebrospinal fluid. Claims 13-15 properly depend from claim 12, and necessarily contain all of the limitations set forth in this independent claim.

The cited references, alone or in combination, do not disclose or suggest every element of the claimed composition. The Kim reference does not disclose or suggest a composition having a first polymer particle having a first therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and a second polymer particle having a second therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil, and wherein the composition is controllably buoyant within the cerebrospinal fluid. Moreover, the Ouadji reference fails to describe the claim limitations that are missing in Kim.

The Examiner states that it would have been obvious to a person of ordinary skill to use two different polymer particles, each containing a different therapeutic agent, because Kim teaches that antibodies can be used in combination with other therapeutic agents. Modulating the ratio of the quantities of the first and second polymer particles is essentially modifying the

dosages of the therapeutic agents contained within each particle. Office Action at pages 16 and 17.

Applicants disagree. The mere fact that the prior art could be so modified does not render the modification obvious unless the prior art suggested the desirability of the modification *In re Laskowski*, 871 F.2d 115, 117, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989) (quoting *In re Gordon*, 733 F.2d 900, 902, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984). The fact that the Kim compositions can be used in combination with other therapeutic agents, without more, does not render the composition of claim 12 obvious. There must be a suggestion or motivation for one to generate a composition comprising two different controllably buoyant microspheres, each of which contains a therapeutic agent and a buoyancy agent.

In moving from the prior art to the claimed invention, one cannot base a determination of obviousness on what the skilled person might try or find obvious to try. Rather, the proper test requires determining what the prior art would have led the skilled person to do. Kim alone, or the combination of Kim and Ouadji does not lead the skilled artisan to generate the composition of claim 12.

Accordingly, Applicants submit that a *prima facie* case of obviousness has not been established. As such, withdrawal of this rejection is requested.

Claim 22

As amended, claim 22 recites a method for administering a therapeutic agent within the central nervous system of a subject, the method comprising intrathecally administering a composition to the central nervous system of said subject, wherein said composition comprises a biodegradable polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and the composition is controllably buoyant within the cerebrospinal fluid. Claims 24-30 depend from claim 22 and necessarily contain all of the limitations set forth in this independent claim.

The primary reference does not disclose or suggest a method for administering a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and the composition is controllably buoyant within the cerebrospinal fluid to the CSF of a patient. The Ouadji reference fails to describe these claim elements.

Kim does not describe the use of a gaseous buoyancy agent contained within a polymeric, particle, and moreover, controllable buoyancy is not suggested by Kim or the cited combination of references. Kim simply discloses a polymeric dispersion system for use in the CNS. There is no disclosure to point one skilled in the art to the desirability of controlling the buoyancy of the dispersion system. There is no teaching or suggestion of the desirability of modulating, or even considering, the density of the formed particles relative to the CSF. Further, there is no reason for one to look to the Ouadji art of improving the bioavailability of agents in the GI tract for guidance as to how to modify the density of agents for administration to the CNS. The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. *Alza Corp. v. Mylan Laboratories Inc.*, 391 F.3d 1365, 1372-1373 (Fed. Cir. 2004), and such a suggestion or motivation is not present in either of the cited references.

Kim, Ouadji, and Chen

Claim 11 was rejected under 35 U.S.C. 103 as being unpatentable over U.S. Patent 5,455,044 ("Kim") in view of U.S. Patent Publication US2003/0138486 A1 ("Ouadji") further in view of Chen et al., PNAS, 2002, 99:9031-9036 ("Chen"). Claim 11 depends from claim 1.

According to the Examiner, Chen teaches the administration of inosine to rats with unilateral cortical infarcts (Office Action at page 17) and that inosine may represent a novel approach to improving function after stroke or CNS trauma (Office Action at page 18). The Examiner further states that it would have been obvious to a person of ordinary skill in the art to combine the teachings of Kim & Ouadji with those of Chen in a therapeutic composition intended for the treatment of a neurological disorder resulting from stroke or CNS trauma because inosine stimulates axonal rewiring...and the combined teachings of Kim and Ouadji teach dispersible pharmaceutical compositions with sustained release properties for the treatment of neurological disorders." Office Action at page 18.

Applicants disagree. As amended, claim 1 recites a biocompatible composition comprising a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and the composition is controllably buoyant within the cerebrospinal fluid (CSF). Claim 11, which properly depends from claim 1

and necessarily contains all of the limitations set forth in this independent claim, specifies that the therapeutic agent is selected from inosine, citicholine, superoxide dismutase, and dextrorphan.

As discussed above, the Kim and Ouadji references alone, or in combination, do not disclose or suggest every element of the claimed composition. Chen does nothing to cure this deficiency. There is no mention in any of these references of a polymer particle having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and the composition is controllably buoyant within the cerebrospinal fluid. Chen simply indicates that inosine might be a useful therapeutic agent for treating a CNS disorder.

For all the foregoing reasons, the rejection should be withdrawn.

Kim, Ouadji, Chen, and Hatcher

Claim 32 was rejected under 35 U.S.C. 103 as being unpatentable over U.S. Patent 5,455,044 ("Kim") in view of U.S. Patent Publication US2003/0138486 A1 ("Ouadji") further in view of Chen et al., PNAS, 2002, 99:9031-9036 ("Chen") and further in view of Hatcher et al., Society for Neuroscience, 19th annual Meeting, Abstract #236.4, Oct.23-28, 1999 (Hatcher). Claim 32 depends from claim 1.

According to the Examiner, Hatcher teaches that CDP-choline (citicholine) decreased neuronal death and provided slight neuroprotection. Office Action at page 19. The Examiner further states that it would have been obvious to a person of ordinary skill at the time of the instant invention to use inosine and citicholine in the same pharmaceutical composition for the treatment of neurological disorders. Office Action at pages 19 and 20.

Applicants disagree.

As amended, claim 12 recites a composition comprising a first polymeric particle having a first therapeutic agent and a buoyancy agent contained therein, and a second polymeric particle having a second therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agents are each a gas or an oil, and the composition is controllably buoyant within the cerebrospinal fluid. Claim 32, which properly depends from claim 12 and necessarily contains all of the limitations set forth in this independent claim, specifies that the first therapeutic agent is inosine and that the second therapeutic agent is citicholine.

As discussed above, the Kim, Ouadji, and Chen references alone, or in combination, do not disclose or suggest every element of the claimed composition. Hatcher does nothing to cure this deficiency. There is no mention in any of these references of a composition having a first polymer particle having a first therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil and a second polymer particle having a second therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is a gas or an oil, and wherein the composition is controllably buoyant within the cerebrospinal fluid.

The fact that the Kim or Ouadji compositions can be used in combination with other therapeutic agents, without more, does not render the composition of claim 12 obvious. There must be a suggestion or motivation for one to generate a composition comprising two different controllably buoyant microspheres, each of which contains a therapeutic agent and a buoyancy agent. Chen simply indicates that inosine might be a useful therapeutic agent for treating a CNS disorder, and Hatcher simply indicates that citicholine might be a useful therapeutic agent for treating a CNS disorder. Assuming *arguendo* that combinations of citicholine and inosine are obvious from the combined teachings of Chen and Hatcher, there is nothing in Kim and/or Ouadji that teaches or suggests a composition of two types of controllably buoyant polymer particles as specified in claim 12.

For all the foregoing reasons, the rejection should be withdrawn.

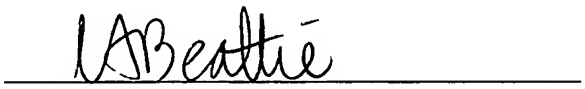
VIII. Other Matters

The Examiner suggests that Applicants insert a sentence in the Abstract that recites the essential components of the claimed composition. Applicants have herein presented an amended Abstract. The Examiner also suggested using a complete name for terms abbreviated in the claims. Applicants have amended the claims accordingly.

CONCLUSION

On the basis of the foregoing, Applicants respectfully request that the rejection of the pending claims be withdrawn. If there are any questions regarding these remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



Ingrid A. Beattie (Reg. No. 42,306)
Attorney for Applicants
c/o MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY AND POPEO, P.C.
Telephone: (617) 542-6000
Customer No. 30623

Appendix

Amended Figure 2 is included herein.